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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/551,152	09/25/2006	Xin-Yun Huang	2003080-0205 (SK-1071-US2)	4442
63411 7590 02/01/2010 CHOATE, HALL & STEWART LLP SLOAN-KETTERING INSTITUTE FOR CANCER RESEARCH TWO INTERNATIONAL PLACE BOSTON, MA 02110			EXAMINER HAVLIN, ROBERT H	
			ART UNIT 1626	PAPER NUMBER
			MAIL DATE 02/01/2010	DELIVERY MODE PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. 10/551,152	Applicant(s) HUANG ET AL.	
	Examiner ROBERT HAVLIN	Art Unit 1626	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 21 October 2009.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-42 and 45-47 is/are pending in the application.
- 4a) Of the above claim(s) 13, 15, 21-26, 28, 29 and 31-40 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-12, 14, 16-20, 27, 30, 41, 42 and 45-47 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 28 September 2005 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date <u>10/21/09</u> . | 6) <input type="checkbox"/> Other: _____ |

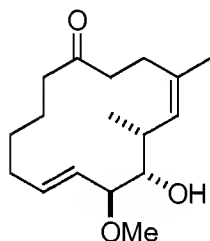
DETAILED ACTION

Status of the claims: Claims 1-42 and 45-47 are currently pending.

Priority: This application is a 371 of PCT/US04/09380 (03/26/2004) which claims benefit of 60/458,827 (03/28/2003) and claims benefit of 60/496,165 (08/19/2003).

Election/Restrictions

1. Applicant previously elected the following species (stated to read on claims 1-12, 14, 16-20, 27, 30, 41-62):



As detailed in the following rejections, the generic claim encompassing the elected species was not found patentable. Therefore, the provisional election of species is given effect, the examination is restricted to the elected species only, and claims not reading on the elected species are held withdrawn. Accordingly, claims 13, 15, 21-26, 28, 29, 31-40 are hereby withdrawn.

Should applicant, in response to this rejection of the Markush-type claim, overcome the rejection through amendment, the amended Markush-type claim will be reexamined to the extent necessary to determine patentability of the Markush-type claim. See MPEP § 803.02.

Applicant correctly points out that certain claims were erroneously included in statements of rejection when they were, in fact, withdrawn. Claims 1-12, 14, 16-20, 27,

30, 41-42, and 45-47 were the only claims under consideration in the prior office action as was indicated in the telephonic interview of 10/13/2009.

RESPONSE TO APPLICANT REMARKS

Claim Rejections - 35 USC § 102

2. Claims 1-11, 16, and 27 were rejected under 35 U.S.C. 102(b) as being anticipated by Singh et al. (Indian Journal of Chemistry, Section B: Organic Chemistry Including Medicinal Chemistry (2002), 41B(2), 423-426).

Applicant has deleted the alternative of R6 is hydrogen, thus the claims are now distinguished from the prior art. Accordingly, the rejection is **withdrawn**.

Claim Rejections - 35 USC § 112

3. Claims 1-12, 14, 16-20, 27, 30, 41-42, and 45-47 were rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Applicant has amended the claims to make the dosage clear in that it refers to a compound of formula I. Therefore, this rejection is **withdrawn**.

4. Claims 1-12, 14, 16-20, 27, 30, 41-42, and 45-47 were rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention due to use of "a therapeutically effective amount" without any reference to a therapy.

Applicant amended the claims to include the phrase "for treating tumor metastases" to indicate the referenced therapy. Therefore, this rejection is **withdrawn**.

NEW CLAIM REJECTIONS NECESSITATED BY AMENDMENT

Claim Rejections - 35 USC § 112

5. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. Claims 1-12, 14, 16-20, 27, 30, 41-42, and 45-47 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the compounds identified as having activity through relevant experimental data, does not reasonably provide enablement for the asserted utility of the entirety of the claim scope, in particular for treating tumor metastases. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

Particularly relevant to the instant case is the issue as to whether the specification provides embodiments allowing use of the claimed invention without requiring undue experimentation by one of ordinary skill in view of the highly unpredictable nature of treating tumors with pharmaceuticals.

“[An inventor] must not be permitted to achieve . . . dominance by claims which are insufficiently supported and hence not in compliance with the first paragraph of 35 U.S.C. 112. That paragraph requires that the scope of the claims must bear a reasonable correlation to the scope of enablement provided by the specification to persons of ordinary skill in the art. In cases involving predictable factors, such as mechanical or electrical elements, a single embodiment provides broad enablement in the sense that, once imagined, other embodiments can be made without difficulty and their performance characteristics predicted by resort to known scientific laws. In cases involving unpredictable factors, such as most chemical reactions and physiological activity, the scope of enablement obviously varies inversely with the degree of unpredictability of the factors involved.” *In re Fisher*, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970).

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Accordingly, the critical element here how broad the claims are compared to the level of unpredictability in the art.

The test of enablement is whether one skilled in the art could make and use the claimed invention from the disclosures in the specification coupled with information known in the art without undue experimentation (*United States v. Teletronics*, 8 USPQ2d 1217 (Fed. Cir. 1988)). Whether undue experimentation is needed is not based upon a single factor but rather is a conclusion reached by weighing many factors. These factors were outlined in *Ex parte Forman*, 230 USPQ 546 (Bd. Pat. App. & Int. 1986) and again in *In re Wands*, 8 USPQ2d 1400 (Fed. Cir. 1988) and include the following:

Nature of Invention. The nature of the invention involves pharmaceutical compounds (migrastatin analogs) for treating tumor metastases.

Scope of the Invention. The scope of the invention is for a genus of compounds of formula I having in excess of millions of species.

State of the Art and Level of Skill in the Art. Although the level of skill in the art is very high, treating tumors is a very unpredictable art and migrastatin was only recently discovered as having this property. The mechanism of action of migrastatin itself was not known at the time of filing and as demonstrated in numerous prior arts, this area of research was completely unpredictable. For example, in Table 1 of Njardarson et al. (cited in IDS J. Amer. Chem. Soc., 2004, 126, 1038-1040), the IC₅₀ values of the various derivatives vary by more than three orders of magnitude. Thus, it is clear that this art is entirely unpredictable, and those of skill in the art would not be able to determine which compounds possessed activity without undue experimentation.

Number of Working Examples and Guidance Provided by Applicant. The applicant provides experimental data in the figures for 3 compounds: macrolactone 48, 55, and macroketone 60 and a few others of questionable relevance to the present claim scope. If applicant intends to rebut this conclusion, the examiner requests a listing of relevant compounds along with the associated experimental data showing the ability to treat tumor metastases.

Unpredictability of the Art and Amount of Experimentation. The art of using compounds to treat tumors is highly unpredictable as described by Njardarson et al. In nearly every case, the skilled artisan could not predict *a priori* whether a given compound would affect a tumor. When small variations in structure such as shown in table 1 of Njardarson has radical effects on the IC₅₀ values, without specific guidance or correlations indicating how the structure of species affects its utility, the scope of enablement is constrained to compounds showing substantial similarity to those actually demonstrated to be useful. Furthermore, there would be a huge amount of undue

experimentation required in order to synthesize and screen the millions of compounds within the claimed scope.

Considering the above factors, the claims are not enabled for the full scope of the compounds claimed. The examiner recommends either amending the claim scope to only those compounds closely resembling the compounds actually tested and disclosed in the specification or provide additional data and/or structural correlations to guide one of ordinary skill in the art to compounds possessing the asserted utility.

Conclusion

The claims are not in condition for allowance. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Correspondence

Any inquiry concerning this communication or earlier communications from the examiner should be directed to ROBERT HAVLIN whose telephone number is (571)272-9066. The examiner can normally be reached on Mon. - Fri., 7:30am-5pm EST.

If attempts to reach the examiner by telephone are unsuccessful the examiner's supervisor, Joe McKane can be reached at (571) 272-0699. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>.

Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Robert Havlin/
Examiner, Art Unit 1626

/Rebecca L Anderson/
Primary Examiner, Art Unit 1626